



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Kevin R. Stone et al.  
Serial No.: 10/665,844  
Filing Date: September 19, 2003  
Title: Anterior Cruciate Ligament Xenographs  
Docket: CROL-0114CP2CN3

\*\*\*\*\*  
CERTIFICATE OF EXPRESS MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee," Express Mail Label No. EV 961806276 in an envelope addressed to MS: Petition, Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450, on October 19, 2006.

Elsie Saraglow  
Elsie Saraglow

MS: Petition  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**PETITION TO REVIVE**

Dear Sir:

Applicants hereby petition for withdrawal of the Notice of Abandonment for the above-captioned application.

Applicants received a Notice of Abandonment, mailed September 19, 2006, indicating the above-captioned application was abandoned because of failure to respond to the Office Action mailed on January 17, 2006.

Applicants submitted a Response to Office Action on July 17, 2006. Attached herewith is a copy of the Transmittal Letter, Response to Office Action, Exhibit A, Exhibit B, Petition for Three-Month Extension of Time, U.S. Patent and Trademark date-stamped postcard receipt, and date-stamped Express Mail Label, indicating these items were timely filed on July 17, 2006.

In view of the foregoing, Applicants respectfully request withdrawal of abandonment.

Although Applicants do not believe a fee is due with the filing of this paper, the Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment, to Deposit Account No. 50-3431. A duplicate of this sheet is enclosed.

Respectfully submitted,  
Foley & Lardner LLP  
Customer No. 48329

\_\_\_\_\_  
Mark G. Lappin, Reg. No. 26,618

Date: October 19, 2006

111 Huntington Avenue  
Boston, MA 02199  
Telephone: (617) 342-4000; Fax: (617) 343-4001



Express Mail No. EV 426288090 US  
Date Mailed: July 17, 2006  
Serial No.: 10/665,844  
Inventor: Kevin R. Stone, et al.  
Title: Anterior Cruciate Ligament Xenografts

Affidavit/Declaration  
 Response (5 Pages)  
 Application; \_\_\_\_\_ Pages  
 Claims ( \_\_\_\_\_ Pages)  
 Appeal, Notice of  
 Assignment with recordation cover sheet  
  
 Brief (in triplicate)  
 Declaration & Power of Attorney  
 Design Application  
 Disclaimer  
 Disclosure Statement with Form-1449  
w/refs.  w/o refs.  
 Drawings  
\_\_\_\_ Sheets \_\_\_\_ Figures



First Class Mail

Filing Date: 09/19/2003

Fee Address Indication Form  
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 Issue Fee Transmittal  
 Notice to File Missing Parts (copy)  
 Response to Not. to File Missing Parts  
 Petition for Extension of Time (1 page)  
(in duplicate) (3 months)  
 Pet. Under 37 C.F.R. \_\_\_\_\_  
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Address Change  
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Other: Exhibits A and Exhibit B CROL-114CP2CN3 (91957-010205) BY: MGL

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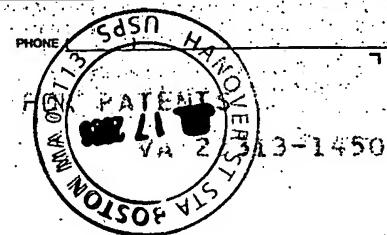
M. G. Lappin

LCR01-0114CP2CN3 (91957-010205)

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PATENT

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In re Application of: Kevin R. Stone et al.  
Serial No.: 10/665,844  
Filing Date: September 19, 2003  
Title: Anterior Cruciate Ligament Xenographs  
Docket: CROL-0114CP2CN3 (91957-010205)

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Ben Joplin  
Ben Joplin

\*\*\*\*\*  
**MS: Amendment**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**TRANSMITTAL LETTER**

Dear Sir:

Enclosed herewith for filing in connection with the above-identified patent application are the following:

1. Response to Office Action (5 pages);
2. Exhibit A (2 pages);
3. Exhibit B (2 pages)
4. Petition for Three-Month Extension of Time (1 page) (in duplicate); and
5. Return Postcard.

The Commissioner is hereby authorized to charge \$510.00 for Three-Month Extension of Time fee, and any additional fees which may be required, or credit any overpayment, to Deposit Account No. 50-2678. A duplicate of this sheet is enclosed.

Respectfully submitted,  
Greenberg Traurig, LLP  
Customer No. 35893

David J. Dypen Reg. No. 46,678 for  
Mark G. Lappin, Reg. No. 28,618  
One International Place  
Boston, MA 02110  
Telephone: (617) 310-6010, Fax: (617) 310-6001

Date: July 17, 2006

**EXHIBIT A**

[All Databases](#)[PubMed](#)[Nucleotide](#)[Protein](#)[Genome](#)[Structure](#)[OMIM](#)[PMC](#)[Journals](#)[Books](#)[Search PubMed](#)[for](#)[\[Go\]](#) [\[Clear\]](#)[Limits](#) [Preview/Index](#) [History](#) [Clipboard](#) [Details](#)Display [Abstract](#)[Show](#) [20](#)[Sort by](#)[Send to](#)[About Entrez](#)[Text Version](#)[Entrez PubMed](#)[Overview](#)[Help | FAQ](#)[Tutorials](#)[New/Noteworthy](#) [E-Utilities](#)[PubMed Services](#)[Journals Database](#)[MeSH Database](#)[Single Citation Matcher](#)[Batch Citation Matcher](#)[Clinical Queries](#)[Special Queries](#)[LinkOut](#)[My NCBI](#)[Related Resources](#)[Order Documents](#)[NLM Mobile](#)[NLM Catalog](#)[NLM Gateway](#)[TOXNET](#)[Consumer Health](#)[Clinical Alerts](#)[ClinicalTrials.gov](#)[PubMed Central](#)[\[1\]: Transplantation. 1995 Oct 27;60\(8\):841-7.](#)[Related Articles, Links](#)

**Enzymatic removal of alpha-galactosyl epitopes from porcine endothelial cells diminishes the cytotoxic effect of natural antibodies.**

**LaVecchio JA, Dunne AD, Edge AS.**

Department of Molecular and Cellular Biology, Diacrin Inc., Charlestown, Massachusetts 02129, USA.

Xenotransplantation of tissues between discordant species such as pig into human is not yet feasible due to the problem of hyperacute rejection. This rapid response to xenogeneic tissue is mediated by natural antibodies that react with antigens on the xenograft. A number of xenoantigens consist of carbohydrate residues, and a terminal galactose in alpha linkage has been shown to be involved in hyperacute rejection of pig-to-human xenografts. We show that alpha-linked galactose on porcine endothelial cells is a major epitope recognized by IgG and IgM antibodies present in monkey and human sera. Endothelial cells that had been treated with alpha-galactosidase did not react with fluorescein-labeled Griffonia simplicifolia I B4 (GS-IB4), a lectin that detects the alpha-galactosyl epitope on intact cells. The reactivity of both human and cynomolgus monkey serum with endothelial cells was decreased by 59% to 90% after treatment with coffee bean alpha-galactosidase. Using a colorimetric assay for cell viability, we show that natural antibodies present in the sera of cynomolgus monkey and humans are cytotoxic to porcine endothelial cells in the presence of exogenously added complement. When the terminal alpha-galactosyl residues were removed by enzymatic digestion, the cytotoxic effect of natural antibodies on porcine endothelial cells was diminished by > 80%. Evaluation of the time course of reappearance of the alpha-galactosyl epitope at the cell surface revealed that 48 hr after alpha-galactosidase treatment, binding of GS-IB4 was diminished by 60%. These results suggest that glycosidase treatment of cells to be transplanted could prevent hyperacute rejection mediated by natural antibodies.

**PMID: 7482745 [PubMed - indexed for MEDLINE]**

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**EXHIBIT B**



Subst. Form PTO-1449				Docket Number (Optional) CROL-114CP2CN	Application Number To be assigned	
INFORMATION DISCLOSURE CITATION IN AN APPLICATION				Kevin R. Stone et al		
				April 2, 2001		
U. S. Patent Documents						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	5,007,934	4/91	Stone			
	5,067,962	11/91	Campbell et al.			
	5,071,741	12/91	Brockbank			
	5,078,744	1/92	Chvapil			
	5,092,894	3/92	Kenny			
	5,116,374	5/92	Stone			
	5,131,850	7/92	Brockbank			
	5,158,574	10/92	Stone			
	5,160,313	11/92	Carpenter et al.			
	5,171,273	12/92	Silver et al.			
	5,171,322	12/92	Kenny			
	5,171,660	12/92	Carpenter et al.			
	5,192,312	3/93	Orton			
	5,216,126	6/93	Cox et al.			
	5,306,304	4/94	Gendler			
	5,306,311	4/94	Stone et al.			
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)						
	Rubak et al., <i>Acta Orthop. Scand.</i> , 53:181-186 (1982).					
	Engkvist, Ove, <i>Scand. J. Plast. Reconstr. Surg.</i> , 13:361-369 (1982).					
	Collins et al., Xenotransplantation, Characterization of Porcine Endothelial Cell Determinants Recognized by Human Natural Antibodies, 1:36-46 (1994).					
	Satake et al., Xenotransplantation, Limited Specificity of Xenoantibodies In Diabetic Patients Transplanted With Fetal Porcine Islet Cell Clusters. Main Antibody Reactivity Against $\alpha$ -linked Galactose-Containing Epitopes, 1:89-101 (1994).					
	LaVecchio et al., Transplantation, Enzymatic Removal of Alpha-Galactosyl Epitopes From Porcine Endothelial Cells Diminishes The Cytotoxic Effect of Natural Antibodies, 60:841-847, (1995)					
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy with next communication to applicant.						



PATENT

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In re Application of: Kevin R. Stone et al.  
Serial No.: 10/665,844  
Filed: September 19, 2003  
Title: Anterior Cruciate Ligament Xenographs  
Examiner: Saucier, Sandra E. Art Unit: 1651  
Atty: Docket: CROL-0114CP2CN3 (91957-010205)

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Ben J  
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**MS: Amendment**  
Commissioner for Patents  
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Alexandria, VA 22313-1450

REQUEST FOR THREE-MONTH EXTENSION OF TIME

Sir:

Pursuant to 37 C.F.R. 1.136(a)(3), applicants hereby petition for a three-month extension of time to respond to the Office Action dated January 17, 2006, in the above-identified application. With the extension, the response is due up to, and including, July 17, 2006. Please charge the fee of \$510.00 based on small entity status, in payment of the fee required by 37 C.F.R. 1.17(a)(3), to our Deposit Account No. 50-2678.

Please charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-2678. A duplicate of this sheet is enclosed.

Respectfully submitted,  
Greenberg Traurig, LLP  
Customer No. 35893

Mark G. Lappin Reg. No. 46,678

Mark G. Lappin, Reg. No. 26,618  
One International Place  
Boston, MA 02110  
Telephone: (617) 310-6010  
Facsimile: (617) 310-6001

Date: July 17, 2006